II. REMARKS

Preliminary Remarks

The applicants would like to thank the examiner for the indication of allowable subject matter in claims 9 and 10.

Upon entry of this Amendment, claims 1, 2, 9, 10, and 26 are pending, of which claims 1, 9, and 26 are independent. Claim 1 is amended to delete the compounds of Groups IA and VA), as well as their sub-groups. Claim 2 is amended to the method of Claim 1, in which R is chosen from groups IIA) and IVA). Claims 5 and 21 to 25 were previously canceled. Claims 3, 4, 6, and 11 to 20 were withdrawn from consideration and are canceled by the current Amendment.

The applicants respectfully request entry of this response pursuant to 37 C.F.R. §1.116, in that if the examiner maintains the claim rejections, this response places the claims in better form for appeal. This response is filed within the statutory period for response and is accompanied by a petition for a one-month extension of time and the appropriate fees. The applicants respectfully request reconsideration and allowance of the present application.

Patentability Remarks

Rejection under 35 U.S.C. §103 –

Claims 1 to 2 were rejected under 35 U.S.C. §103(a) as being unpatentable over Scherrer *et al.* (U.S. Pat. No. 3,313,848) and Matji *et al.* (WO 94/04484) in view of Persson *et al.* (CA 117:45429) and Chung *et al.* (CA 125:105692). The applicants respectfully traverse in view of the preceding amendments and succeeding remarks.

The examiner alleges that Scherrer *et al.* and Matji *et al.* describe compounds similar to those claimed for treating inflammation, while Persson *et al.* and Chung *et al.* teach NO donors for increasing time to micturition and bladder pressure threshold, and therefore, the disclosed compounds are known to be useful for treating urinary incontinence.

Claims 1 and 2, as amended, exclude any compounds described in either Scherrer *et al.* or Matji *et al.* With respect to the remaining compounds, the applicants respectfully direct the examiner's attention to The Merck Index, 13th Ed., Therapeutic Category and Biological Activity Index (enclosed), which shows that flurbiprofen is an anti-inflammatory nonsteroidal drug, arylpropionic acid derivative.

NO-flurbiprofen belongs to group IIA) of claim 1 and the applicants respectfully submit that it is representative of all the arylpropionic acid derivatives falling within groups IIA) and IIIA), including suprofen (Formula II), carprofen (XXI), ketoprofen (IV), fenoprofen (VII), thiaprofenic acid (XXXV), indoprofen (VI), flurbiprofen (IX); pranoprofen (IIIa), bermoprofen (XXX), CS-670 (XXXI), zaltoprofen (XXXVI), naproxen (II), loxoprofen (X), and ibuprofen (III).

All the compounds above reported belong to the same therapeutically class, i.e. anti-inflammatory nonsteroidal drugs and containing $-CH(CH_3)-COOH$. Therefore, NO-flurbiprofen is representative of this class of compounds.

Furthermore, the present invention is concerned with the administration of compounds $A-X_1-NO_2$ as claimed, for the treatment of urinary incontinence. Persson *et al.* and Chung *et al.*, however, teach that the disclosed NO donors require electric stimulation or UV light to work. Accordingly, those of ordinary skill in the art would have no motivation to combine the NO donors of Persson *et al.* and Chung *et al.* with the compounds of Scherrer *et al.* and Matji *et al.* for the treatment of urinary incontinence as claimed. Indeed, due to the necessity of electric stimulation or UV light, those of ordinary skill in the art would have no motivation to combine reference teachings, so as to arrive at the claimed method (Manual of Patent Examining Procedure §2143.01).

In order for the examiner to set forth a *prima facie* case of obviousness he is required to consider each reference as a whole, taking into account all teachings disclosed therein. It is impermissible to pick and choose only those teachings that might support a rejection. The applicants respectfully submit that the examiner has engaged in just such an impermissible picking and choosing of reference teachings.

The combination of reference teachings as a whole, would result in inoperative NO donors. The claimed method does not envision electric stimulation or UV light, and

those of ordinary skill in the art would recognize that patients in such a treatment could not be electrically stimulated or UV illuminated during the administration of the claimed compounds. In contrast, in Persson *et al.* and Chung *et al.*, electric stimulation or UV light is introduced during *in vitro* experiments on small strips of rat/pig muscle. Clearly, this is something other than the claimed invention, and provides no motivation concerning the method of treatment claimed.

The applicants respectfully submit that claims 1 and 2 are not unpatentable over Scherrer *et al.* and Matji *et al.* in view of Persson *et al.* and Chung *et al.* and request withdrawal of this rejection.

Finally, the applicants respectfully draw the examiner's attention to claim 26. This claim was added in the Supplemental Preliminary Amendment filed on September 8, 2003. As this claim is not the subject of any rejections, the applicants believe that it is allowable.

III. CONCLUSION

In view of the amendments and remarks above, the applicants respectfully submit that this application is in condition for allowance and request favorable action thereon.

In the event this response is not timely filed, the applicants hereby petition for an appropriate extension of time. The fee for this extension, along with any other additional fees which may be required with respect to this response, may be charged to Deposit Account No. 01-2300, referencing Attorney Docket No. 026220-00031.

Respectfully submitted,

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Acemetacin, *28*
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Amfenac, *395*
Amtolmetin Guacil, *600*
Bromfenac, *1374*
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Indomethacin, *4990*
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Indoprofen, *4991*
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Pyrazolones
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